ADIR 360/lw

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Applicants : Gilbert LAVIELLE, Olivier MULLERM, Mark MULLAN, Anne DEKEYNE, and Mauricette BROCCO

Title : New Diphenylureal compounds

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Honorable Commissioner of Patents and Trademarks
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Sir:

As soon as the Serial No. and Filing Date have been accorded the above-identified application, kindly enter the following amendment:

IN THE ABSTRACT: Kindly replace the Abstract, page 47 and 48, with the substitute Abstract sheet page 6 provided herewith.

IN THE CLAIMS: Kindly cancel claims 1-17 and replace with the following claims 18-34, which correspond to each cancelled claim.

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REMARKS:

A few constructive editorial changes have been made in the claims to bring them somewhat more into line with U.S. practice and requirements.

Applicants have cancelled all of the originally filed claims, 1-17. New claims 18-34 have been added to better encompass the full scope and breadth of the invention, notwithstanding Applicants' belief that the claims would have been allowable as originally filed. Accordingly, Applicants assert that no claims have been narrowed within the meaning of Festo .

Entry of the amendments and favorable action on the merits are all hereby respectfully solicited.

Respectfully submitted,

THE FIRM OF HUESCHEN AND SAGE

G. PATRICK SAGE, Attorney #37,710

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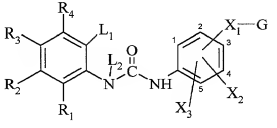
CLAIMS

We claim :

18. A compound selected from those of formula (I) :



(I)

wherein

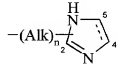
- ✓ R_1, R_2, R_3 and R_4 independently represent hydrogen, halogen or alkyl, alkoxy, hydroxy, alkylthio, mercapto, cyano, amino (optionally substituted by one or two alkyl), nitro, carboxy, alkoxycarbonyl, aminocarbonyl (optionally substituted by one or two alkyl groups) or carbamoyl,
  or, taken in pairs, form together with the carbon atoms to which they are bonded a phenyl ring or an aromatic heterocycle having from 5 to 7 ring members and containing from 1 to 3 hetero atoms selected from nitrogen, oxygen and sulphur,

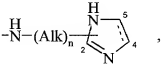
- ✓ L_1 and L_2 each represents hydrogen or together form $-CH_2-CH_2-$,

- ✓ X_1, attached at the 2 or 3 position of the aromatic ring, represents a bond, and in that case X_2 represents hydrogen, halogen, alkyl, alkoxy, hydroxy, nitro or cyano, or amino (optionally substituted by one or two alkyl groups),
  or,
  X_1 and X_2, together with two adjacent carbon atoms to which they are bonded in the 2, 3 or 4 position of the aromatic ring, form (C_4-C_7)cycloalkyl wherein one or two $-CH_2-$ of the cycloalkyl ring are optionally replaced by oxygen or NH (optionally substituted by alkyl) and wherein one carbon of the cycloalkyl ring is substituted by G,

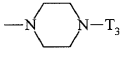
- ✓ X_3 represents hydrogen, halogen, alkyl, alkoxy, hydroxy, nitro or cyano, or amino (optionally substituted by one or two alkyl groups),

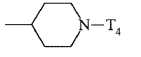
- ✓ G represents a group selected from :



,  ,

G_1 G_2



and  ,

G_3 G_4

wherein :

- ✓ the broken lines indicate the optional presence of a double bond,

- ✓ Alk represents linear or branched (C_1-C_6)alkylene wherein, when G_1 or G_2 contains imidazoline, the group Alk- is attached at the 2 position of the ring,

- ✓ n is 0 or 1,

- ✓ T_3 represents alkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl or optionally substituted heteroarylalkyl,

- ✓ T_4 represents alkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl or optionally substituted heteroarylalkyl,

wherein :

- the term "alkyl" denotes a linear or branched group containing from 1 to 6 carbon atoms,

- the term "alkoxy" denotes a linear or branched alkyl-oxy containing from 1 to 6 carbon atoms,
- the term "aryl" denotes a phenyl, naphthyl or biphenyl group,
- the term "heteroaryl" denotes an aromatic monocyclic group, or a bicyclic group in which at least one of the rings is aromatic, each group containing from 5 to 11 ring members and from 1 to 5 hetero atoms selected from nitrogen, oxygen and sulphur,
- the expression "optionally substituted" associated with aryl, arylalkyl, heteroaryl and heteroarylalkyl denotes that those groups are unsubstituted or substituted on the cyclic moiety by one or more halogen and/or alkyl, alkoxy, hydroxy, mercapto, alkylthio, cyano, amino (optionally substituted by one or two alkyl group), nitro, carboxy, alkoxycarbonyl, aminocarbonyl (optionally substituted by one or two alkyl group) or carbamoyl, wherein heteroaryl and heteroarylalkyl may in addition be substituted by oxo, its

enantiomers and diastereoisomers thereof, and addition salts thereof with a pharmaceutically acceptable acid or base.

19. A compound of claim 18, wherein L_1 and L_2 each represents hydrogen .

20. A compound of claim 18, wherein L_1 and L_2 together form $-CH_2-CH_2$.

21. A compound of claim 18, wherein R_1 and R_4 each represents hydrogen .

22. A compound of claim 18, wherein R_2 and R_3 are selected from halogen and alkyl .

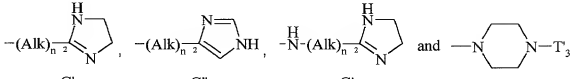
23. A compound of claim 18, wherein X_1 is attached at the 2 position of the phenyl ring .

24. A compound of claim 18, wherein X_1 represents a bond and X_2 represents halogen or alkyl or alkoxy .

25. A compound of claim 18, wherein X_3 represents hydrogen .

26. A compound of claim 18, wherein R_3 and R_4, together with carbon to which they are bonded, form a phenyl ring and L_1 and L_2 together form $-CH_1-CH_2-$.

27. A compound of claim 18, wherein G is selected from :



G'_1 G''_1 G'_2 G'_3

wherein T'3 is an optionally substituted heteroaryl or optionally substituted heteroarylalkyl.

28. A compound of claim 18, wherein X_1 and X_2, together with two carbon atoms in the 2 and 3 position of the aromatic ring to which they are bonded, form (C_4-C_7)cycloalkyl .

29. A compound of claim 18 that is *N*-(3-chloro-4-methylphenyl)-*N'*-{3-[4-(2,3-dihydro-1,4-benzodioxin-2-ylmethyl)-1-piperazinyl]phenyl}urea, its enantiomers and diastereoisomers thereof, and addition salts thereof with a pharmaceutically acceptable acid or base .

30. A compound of claim 18 that is *N*-[4-chloro-3-(4,5-dihydro-1*H*-imidazol-2-ylamino) phenyl]-*N'*-(3-chloro-4-methylphenyl)urea, its enantiomers and diastereoisomers thereof, and addition salts thereof with a pharmaceutically acceptable acid or base .

31. A compound of claim 18 that is *N*-(3-chloro-4-methylphenyl)-*N'*-[2-(1H-imidazol-4-yl)-indan-5-yl]urea, its enantiomers and diastereoisomers thereof, and addition salts thereof with a pharmaceutically acceptable acid or base .

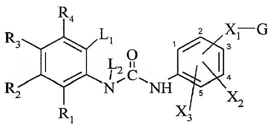
32. A compound of claim 18 that is *N*-{3-[4-(2,3-dihydro-1,4-benzodioxin-2-ylmethyl)-1-piperazinyl]phenyl}-*N'*-(3,4-dimethylphenyl)urea, its enantiomers and diastereoisomers thereof, and addition salts thereof with a pharmaceutically acceptable acid or base .

33. A method for treating an animal or human living body afflicted with a condition which is treatable with a dual α_2/5-HT_{2c} antagonist comprising the step of administering to the living body an amount of a compound of claim 18 which is effective for alleviation of said condition .

34. A pharmaceutical composition useful for treating an animal or humrn living body afflicted with a condition which is treatable with a dual α_2/5-HT_{2c} antagonist comprising a compound of claim 18 in combination with one or more pharmaceutically acceptable, excipients or vehicles .

ABSTRACT OF THE DISCLOSURE

Compounds of formula (I) :



(I)

and medicinal products containing the same which are useful as dual α_2/5-HT_{2c} antagonists.